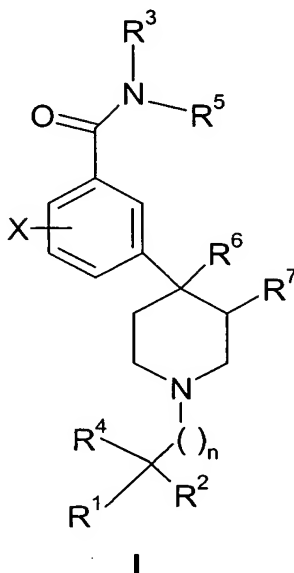


Claims:

1. A compound according to formula I:



wherein X is H, halogen, or CN;

- 5 R¹ and R² are independently H, C₁-C₆ alkyl, -(CH₂)_k-aryl, -(CH₂)_k-heteroaryl, wherein said alkyl, -(CH₂)_k-aryl or -(CH₂)_k-heteroaryl group is optionally substituted anywhere on said group with one or more R¹² groups, or, with the carbon to which R¹ and R² are attached, are connected to form a C₃-C₇ cycloalkyl or a 4-7 membered carbocyclic or heterocycloalkyl comprising from one to three hetero moieties selected from O, S, -C(=O), and N; and wherein
- 10 said cycloalkyl or heterocycloalkyl optionally contains one or more double bonds; and wherein said cycloalkyl or heterocycloalkyl is optionally fused to or substituted with a C₆-C₁₄ aryl or 5-14 membered heteroaryl group; wherein said C₃-C₇ cycloalkyl or 4-7 membered carbocyclic or heterocycloalkyl formed by R¹ and R² can each optionally be substituted by from one to three R¹² groups, and said optionally fused or substituted aryl or heteroaryl, substituted alkyl,
- 15 substituted aryl optionally fused aryl or heteroaryl may each optionally independently be substituted with from one to six R¹² groups in any stereochemical relationship;

- wherein the R¹² groups are independently selected from H, R¹³, R¹⁶, -C₁-C₄ alkyl optionally containing one or two unsaturated bonds, halogen, -OR¹³, -NO₂, -CN, -C₃-C₆ cycloalkyl, aryl, substituted aryl, wherein said aryl or substituted aryl is independently
- 20 optionally substituted with 1-3 R¹⁸ groups, -C(R⁴)(C₁-C₄ alkyl)(C₁-C₄ alkyl) wherein said alkyl groups may form a C₃-C₇ carbocyclic ring, -(CH₂)_v-NR¹³R¹⁴, -NR¹³C(=O)R¹⁴, -C(=O)NR¹³R¹⁴, -OC(=O)R¹³, -C(=O)OR¹³, -C(=O)R¹³, -NR¹³C(=O)OR¹⁴, -NR¹³C(=O)NR¹⁴R¹⁵, -NR¹³S(=O)₂R¹⁴, -NR¹⁷S(=O)₂NR¹³R¹⁴ and -S(=O)₂R¹³;

R^{18} is H, F, Cl, -OH, -C₁-C₄ alkyl, -C≡N, -NR¹³C(=O)R¹⁴, -C(=O)NR¹³R¹⁴, -O(C₁-C₄)alkyl, -NH(C₁-C₄ alkyl), -N(C₁-C₄ alkyl)(C₁-C₄ alkyl), -(CH₂)_nOH, -(CH₂)_n-C≡N, -(CH₂)_n-NR¹³C(=O)R¹⁴, -(CH₂)_n-C(=O)NR¹³R¹⁴, -(CH₂)_n-O(C₁-C₄)alkyl, -(CH₂)_n-NH₂, -(CH₂)_n-NH(C₁-C₄ alkyl) or -(CH₂)_n-N(C₁-C₄ alkyl)(C₁-C₄ alkyl);

5 R^4 is absent or is H, -C₁-C₄ alkyl which may optionally contain one or two unsaturated bonds, -OH, O-(C₁-C₄)alkyl, (C₁-C₄)-alkyl-OH, (CH₂)_nNH₂, -(CH₂)_n-NH(C₁-C₄ alkyl), (CH₂)_n-N(C₁-C₄)alkyl(C₁-C₄)alkyl, -(CH₂)_n-NHC(=O)(C₁-C₄ alkyl), -(CH₂)_n-NO₂, -(CH₂)_n-C≡N, -(CH₂)_n-C(=O)NH₂, -(CH₂)_n-C(=O)NH(C₁-C₄ alkyl) or -(CH₂)_n-C(=O)N(C₁-C₄ alkyl) (C₁-C₄ alkyl), CN, NO₂, -OR¹⁶;

10 R^3 and R^5 are independently H, alkyl C₁-C₆, substituted alkyl C₁-C₆, cycloalkyl C₁-C₆ and substituted cycloalkyl C₁-C₆, (C₂-C₄)alkyl-O-(C₁-C₄)alkyl, (C₂-C₄)alkyl-NH(C₁-C₄ alkyl), (C₂-C₄)alkyl-N(C₁-C₄ alkyl)(C₁-C₄ alkyl), (C₁-C₄)alkyl-heterocyclic;

R^6 and R^7 are independently C₁-C₄ alkyl;

15 each R^{13} , R^{14} , and R^{15} are independently selected from H, -C₁-C₄ alkyl, -(C₂-C₄ alkyl)-O-(C₁-C₄-alkyl), -(CH₂)_v-NR¹⁶R¹⁷, or a 4- to 7-membered heterocyclic group; or R^{13} and R^{14} when in -NR¹³R¹⁴, may optionally be connected to form a 4 to 6 membered heterocyclic group, which heterocyclic group optionally comprises from 1 to 3 further hetero moieties selected from N, S, O and -C(=O);

20 R^{16} and R^{17} are independently H, C₁-C₆ alkyl or together may form a 4- to 7-membered heterocyclic group;

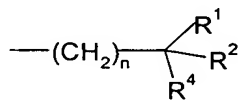
k is an integer selected from zero, 1, 2, 3, 4, and 5; and

v is an integer selected from 2, 3, 4, and 5; and

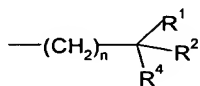
n is an integer selected from zero, 1, 2, 3, 4, and 5;

and pharmaceutically acceptable salts thereof;

25 with the proviso that;



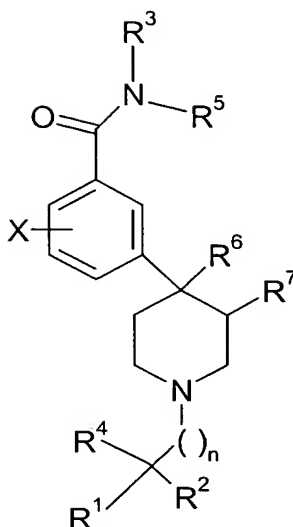
a) in said group, when n is 0, R^1 , R^2 or R^4 cannot be a heteroatom or contain a heteroatom which is directly linked to the carbon of said



group when said carbon is sp³ hybridized; and

b) R^{13} and R^{14} cannot be H in a -NHS(=O)₂R¹⁴ or a -SO₂R¹³ group.

30 2. The compound according to claim 1 represented by the chemical structure II:



II

Wherein each of X, R¹, R², R³, R⁴, R⁵, R⁶, R⁷ and n is represented as described in claim 1 and the preferred relative stereochemistry between R⁶ and R⁷ is *trans*.

3. The compound according to claim 2 wherein R³ and R⁵ are H.
- 5 4. The compound according to claim 2 wherein X is H.
5. The compound according to claim 2 wherein R⁶ and R⁷ are each CH₃.
6. The compound according to claim 2 wherein n is 1, 2 or 3.
7. The compound according to claim 2 wherein R⁴ is OH, CH₂OH, NH₂, NHCOCH₃ or CN.
- 10 8. The compound according to claim 2 wherein R¹ and R² together with the carbon to which they are attached form a carbocyclic group fused to a phenyl group, an unsubstituted or substituted carbocyclic group.
9. The compound according to claim 6 wherein n is 1.
10. The compound according to claim 7 wherein R⁴ is OH.
- 15 11. The compound according to claim 2 wherein R¹ and R² together with the carbon to which they are attached form an indane ring system, a cyclobutane, cyclopentane or cyclohexane group.
12. The compound according to claim 2 wherein R¹ and R² together with the carbon to which they are attached form an indane ring system or a cyclobutane group which is substituted with a phenyl group which is unsubstituted or substituted with one or more R¹² groups.
- 20 13. The compound according to claim 1 wherein R³ and R⁵ are H, X is hydrogen, R⁶ and R⁷ are CH₃, n is 1, R⁴ is OH, CH₂OH, NH₂, NHCOCH₃ or CN and R¹ and R² together

with the carbon to which they are attached, form a carbocyclic group fused to a phenyl ring or an unsubstituted or substituted carbocyclic group.

14. The compound according to claim 2 wherein R³ and R⁵ are H, X is hydrogen, R⁶ and R⁷ are CH₃, n is 1, R⁴ is OH, CH₂OH, NH₂, NHCOCH₃ or CN and R¹ and R² together
5 with the carbon to which they are attached, form a carbocyclic group fused to a phenyl ring or an unsubstituted or substituted carbocyclic group.

15. The compound according to claim 14 wherein R⁴ is OH and R¹ and R² together with the carbon to which they are attached form an indane ring system or a cyclobutane group which is substituted with a phenyl group which is unsubstituted or
10 substituted with one or more R¹² groups.

16. The compound according to claim 14 wherein R⁴ is OH and R¹ and R² together with the carbon to which they are attached form an indane ring system.

17. The compound according to claim 14 wherein R⁴ is OH and R¹ and R² together with the carbon to which they are attached form a cyclobutane group which is
15 substituted with a phenyl group which is unsubstituted or substituted with one or more R¹² groups.

18. The compound:

(+/-)-3-(trans-3,4-Dimethyl-1-phenethyl-piperidin-4-yl)-benzamide;

(+/-)-3-(1-Indan-2-ylmethyl-trans-3,4-dimethyl-piperidin-4-yl)-benzamide;

20 (+/-)-3-{1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl}-
benzamide ;

(+/-)-3-{1-[2-(4-Methoxy-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;

(+/-)-3-{1-[2-(2-Methoxy-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;

(+/-)-3-{1-[2-(3-Methoxy-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;

25 (+/-)-3-{trans-3,4-Dimethyl-1-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperidin-4-yl}-
benzamide ;

(+/-)-3-{1-[2-(4-Cyano-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;

(+)-3-{1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl}-

benzamide ;

30 (-)-3-{1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl}-
benzamide ;

(+/-)-3-{1-[2-(3-Bromo-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;

(+/-)-3-{1-[2-(4-Chloro-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;

(+/-)-3-{1-[2-(3-Chloro-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;

35 (+/-)-3-{1-[2-(3-Cyano-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;

(+/-)-3-{1-[2-(2,6-Dichloro-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide

;

- (+/-)-3-[trans-3,4-Dimethyl-1-(2-pyridin-2-yl-ethyl)-piperidin-4-yl]-benzamide ;
(+/-)-3-[1-(2-Hydroxy-2-phenyl-ethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
(+/-)-3-[1-[3-(1-Cyano-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
5 (+/-)-3-[1-[3-(1-Hydroxy-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
 (+/-)-3-[1-[3-(1-Methoxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
 (+/-)-3-[1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-
10 benzamide ;
 (+)-3-[1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
 (-)-3-[1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
15 (+)-3-[1-(2-Hydroxy-indan-2-ylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-(2-Hydroxy-indan-2-ylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide
mesylate ;
 (+)-3-[1-[2-(2-Hydroxy-indan-2-yl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide
;
20 (+)-3-[1-[2-[3-(1-Hydroxy-cyclohexyl)-phenyl]-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
 (+)-3-[1-(cis-1-Hydroxy-3-phenyl-cyclobutylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
 (+)-2-[2-[4-(3-Carbamoyl-phenyl)-trans-3,4-dimethyl-piperidin-1-yl]-ethyl]-indan-2-
25 carboxylic acid amide ;
 (+)-3-[trans-3,4-Dimethyl-1-[3-(2-nitro-indan-2-yl)-propyl]-piperidin-4-yl]-benzamide ;
 (+)-3-[1-[3-(2-Amino-indan-2-yl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-[cis-3-(4-Bromo-phenyl)-1-hydroxy-cyclobutylmethyl]-trans-3,4-dimethyl-
piperidin-4-yl]-benzamide ;
30 (+)-3-[1-[cis-1-Hydroxy-3-(4-methoxy-phenyl)-cyclobutylmethyl]-trans-3,4-dimethyl-
piperidin-4-yl]-benzamide ;
 (+)-3-[1-[2-(2-Amino-indan-2-yl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
 (+)-3-[1-[2-(2-Acetylamino-indan-2-yl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
35 (+)-2-[2-[4-(3-Carbamoyl-phenyl)-trans-3,4-dimethyl-piperidin-1-yl]-ethyl]-indan-2-
carboxylic acid , or a pharmaceutically acceptable salt of any of the above-listed compounds.

19. (+/-)-3-(trans-3,4-Dimethyl-1-phenethyl-piperidin-4-yl)-benzamide;

(+/-)-3-(1-Indan-2-ylmethyl-trans-3,4-dimethyl-piperidin-4-yl)-benzamide;
(+/-)-3-{1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl}-
benzamide ;
(+/-)-3-{trans-3,4-Dimethyl-1-[2-(3-trifluoromethyl-phenyl)-ethyl]-piperidin-4-yl}-
5 benzamide ;
(+/-)-3-{1-[2-(4-Cyano-phenyl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide ;
(+/-)-3-[1-(2-Hydroxy-2-phenyl-ethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
(+/-)-3-{1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl}-
benzamide ;
10 (+)-3-{1-[3-(1-Hydroxymethyl-cyclopentyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl}-
benzamide ;
(+)-3-{1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl}-
benzamide ;
(-)-3-{1-[3-(1-Hydroxy-cyclohexyl)-propyl]-trans-3,4-dimethyl-piperidin-4-yl}-
15 benzamide ;
(+)-3-[1-(2-Hydroxy-indan-2-ylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide ;
(+)-3-[1-(2-Hydroxy-indan-2-ylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-benzamide
mesylate ;
(+)-(3-{1-[2-(2-Hydroxy-indan-2-yl)-ethyl]-trans-3,4-dimethyl-piperidin-4-yl}-benzamide
20 ;
(+)-3-[1-(cis-1-Hydroxy-3-phenyl-cyclobutylmethyl)-trans-3,4-dimethyl-piperidin-4-yl]-
benzamide ;
(+)-3-{1-[cis-1-Hydroxy-3-(4-methoxy-phenyl)-cyclobutylmethyl]-trans-3,4-dimethyl-
piperidin-4-yl}-benzamide, or a pharmaceutically acceptable salt of any of the above-listed
25 compounds.

20. A pharmaceutical composition comprising an effective amount of a compound according to claim 1 in combination with a pharmaceutically acceptable carrier, excipient or additive.

21. A method of treating in a mammal, in need thereof, a disease state, disorder
30 or condition mediated by an opioid receptor or receptors which method comprises administering to said mammal an amount of a compound according to claim 1, effective in modulating an opioid receptor or receptors.

22. A method of treating in a mammal, in need thereof, a disease state, disorder
or condition selected from the group consisting of irritable bowel syndrome, constipation,
35 nausea, vomiting, pruritic dermatoses, psoriasis; eczema; an insect bite; an eating disorder, depression, anxiety, schizophrenia; drug addiction, an opioid overdose, sexual dysfunction, stroke, head trauma, traumatic brain injury, spinal damage, Parkinson's disease, Alzheimer's

disease, age-related cognitive decline and Attention Deficit and Hyperactivity Disorder which method comprises administering to said mammal an amount of a compound according to claim 1 effective in treating said disease state, disorder or condition.

23. A method of treating in a mammal, in need thereof, a disease state, disorder
5 or condition selected from the group consisting of irritable bowel syndrome, drug addiction, depression, anxiety, schizophrenia and eating disorders which method comprises administering to said mammal an amount of a compound according to claim 1 effective in treating said disease state, disorder or condition.

24. A method of treating in a mammal, in need thereof, a disease state, disorder
10 or condition selected from the group consisting of allergic dermatitis, contact dermatitis, anorexia, bulimia, obesity, alcohol addiction, amphetamine addiction, cocaine addiction, morphine addiction, opium addiction, heroin addiction, erectile dysfunction and impotence, which method comprises administering to said mammal an effective amount of a compound according to claim 1 for treating said disease state, disorder or condition.

25. Use of a compound according to claim 1 in the manufacture of a medicament
15 for the treatment of a mammal.

26. Use of a compound according to claim 1 in the manufacture of a medicament
for the treatment of a mammal, in need thereof, of a disease state, disorder or condition
selected from the group consisting of irritable bowel syndrome, constipation, nausea,
20 vomiting, pruritic dermatoses, psoriasis, eczema; an insect bite; an eating disorder, depression, anxiety, schizophrenia; drug addiction, an opioid overdose, sexual dysfunction, stroke, head trauma, traumatic brain injury, spinal damage, Parkinson's disease, Alzheimer's disease, age-related cognitive decline and Attention Deficit and Hyperactivity Disorder.

27. Use of a compound according of claim 1 in the manufacture of a medicament
25 for the treatment of a mammal, in need thereof, to a disease state, disorder or condition selected from the group consisting of allergic dermatitis, contact dermatitis, anorexia, bulimia, obesity, alcohol addiction, amphetamine addiction, cocaine addiction, morphine addiction, opium addiction, heroin addiction, erectile dysfunction and impotence.

28. A compound according to claim 1 wherein one or more atoms thereof have
30 an atomic mass or mass number different from the atomic mass or mass number usually found in nature, or a pharmaceutically acceptable salt of such compound.

29. A method for obtaining an image of opioid receptors in a mammalian subject,
which method comprises administering to said subject an amount of a compound according to
claim 28, or pharmaceutically acceptable salt thereof, effective in imaging opioid receptors in
35 said subject.